PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hwu et al.

Application No. 09/803,578

Art Unit: 1632

Examiner: Wilson, Michael C.

Filed: March 9, 2001

For: ACTIVATED DUAL SPECIFICITY LYMPHOCYTES AND THEIR METHODS OF USE

DECLARATION UNDER 37 C.F.R. § 1.132 OF DR. PATRICK HWU

1. I, Patrick Hwu, am a co-inventor of the subject matter disclosed and claimed in the above-identified patent application.

2. The data shown in Figures 3A and 3B represent my own work. Figures 3A and 3B demonstrate that the number of Thy 1.1. T-cells in mice increased in response to immunization of the mice with allogeneic splenocytes (Figure 3A) and allogeneic dendritic cells (Figure 3B). The increased number of Thy 1.1 T-cells upon immunization with the allogeneic cells shows that the endogenous T-cell receptors of the Thy 1.1 T-cells reacted to the allogeneic splenocytes or the allogeneic dendritic cells.

3. Examples 4 and 5 represent my own work. Example 5 demonstrates the effect that allogeneic/Mov-γ dual specificity T-cells have on tumors. The dual specificity T-cells were

the dual specificity T-cells generated and tested in Example 4. As shown in Figure 5, tumor-bearing mice that were injected with both allogeneic splenocytes and dual specificity T-cells became tumor-free. The fact that the tumor-bearing mice became tumor-free under these conditions shows that the allogeneic splenocytes reacted with the endogenous T-cell receptors of the dual specificity T-cells, thereby causing the dual specificity T-cells to clonally expand in the mice, which, in turn, allowed the mice to become tumor-free.

4. The data shown in Figures 12A-D represent my own work. Figures 12A-D demonstrate that the number of peripheral blood mononuclear cells (PBMC) responders, which were T-cells, increased upon stimulation with allogeneic PBMC (Figure 12A), allogeneic dendritic cells (DC; Figure 12B), or allogeneic B cells (Figure 12C), in comparison to control cells (Figure 12D). The increased number of PBMC responder cells shows that the endogenous T-cell receptor of the responder cells (T-cells) reacted with the allogeneic PBMC, dendritic cells, or B cells. These PBMC responder cells were retrovirally transduced with nucleic acid molecules encoding the Mov-γ chimeric receptor, such that the cells comprised both a chimeric receptor reactive with a tumor antigen and an endogenous T-cell receptor reactive with an allogeneic cell.

5. I have read Example 4 of U.S. Patent 5,830,755 (herein referred to as the '755 patent). I recognize the work presented in Example 4 as my own work. The cells listed in Table 8 and labeled as "24 JK" or "24 JK FBP" are syngeneic to the cells labeled "38 TIL NV," "38 TNP-TIL," or "38 MOv-γ." That is, the cells are not allogeneic to each other. The release of Interferon-γ by 38 TIL NV cells when stimulated by 24JK cells was not due to an antigenic

distinction between 38 TIL NV cells and the 24JK cells. I know this to be true because these cells are not antigenically distinct from or allogeneic to each other. In this regard, none of the cells listed in Table 8 contain a T-cell receptor that is reactive with an allogeneic cell.

6. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 3/23/05

Patrick Hwu, M.D.